Identification of Immuno-Oncology Crosstalk Pathways in Lung Adenocarcinoma

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Identifying dysregulated pathways from the high throughput data for biomarker detection is the rate limiting step in the complex diseases cure. Pathways don't perform alone; they interact with each other through the overlapping genes. This phenomenon is known as crosstalk of pathways. The aim of the study is develop a methodology to find the highly interacting (cross-talk) immune-oncological pathways and their drug-gene-pathway modules which can be further validated *in-vivo* using Lung Adenocarcinoma (LUAD) as a case study. The reference pathway cross-talk matrix is built using the KEGG Knowledgebase, which consists of the 302 KEGG pathways associated with 6996 genes. The LUAD gene expression data available in The Cancer Genome Atlas (TCGA) is used for the study. The data of 32 patients was used in the study and of these, 9 patients were treated with immunotherapy drugs. A set of 3018 significant genes associated with 296 pathways [*C.I.* =95%, *p-value* <=0.05] are identified in this dataset, and a disease crosstalk matrix is constructed. Each cell in the matrix gives the cross-talk score of the pathways computed using the formula: $\frac{(P_i \cap P_j)_{common\ genes}}{(P_i \cup P_j)_{uniques\ genes}}$. The interaction among the significant genes (3018 genes) in the crosstalk pathways were identified using the BioGrid physical gene-gene interaction map and a gene interaction network (10102 interaction) is generated. The significant genes in the network are annotated to their drugs as given in the clinical data of TCGA. The drug-gene-pathway modules of LUAD are identified using Seed-Based-Network Propagation Algorithm. These modules give the profile of the highest cross-talk pathways of LUAD that can be studied further for alternative drug targets. The study identified T-cell receptor signaling pathway and B cell receptor signaling pathway of LUAD have high crosstalk scores with Erbb Signaling pathway (18.67, 15.15) Vegf signaling pathway (17.77, 22.45); Osteoclast differentiation (16.35, 14.89).